

Hg²⁺-Selective Chemosensor Derived from 8-Hydroxyquinoline Having Benzothiazole Function in Aqueous Environment

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Newly synthesized 8-hydroxyquinoline based benzothiazole derivative **2** showed a distinctive Hg²⁺-selectivity over other transition metal ions in aqueous solution. The fluorescence emission at 455 nm of **2** was completely quenched upon interaction with Hg²⁺ ions in dioxane-H₂O system (9 : 1, v/v). The selectivity was decreased in the order of Hg²⁺ >> Cu²⁺ > Cd²⁺ > Pb²⁺ ≈ Zn²⁺ ≈ Ni²⁺, and Hg²⁺ concentration dependent fluorescence quenching profile was observed in the presence of common interfering metal ions as background. The fluorescence behavior of **2** suggests that the prepared compound could be used as a fluorescent signaling subunit for the construction of new Hg²⁺-sensitive ON-OFF type supramolecular switching systems.

Key Words : 8-Hydroxyquinoline, Benzothiazole, Hg²⁺-selectivity, Fluoroionophore

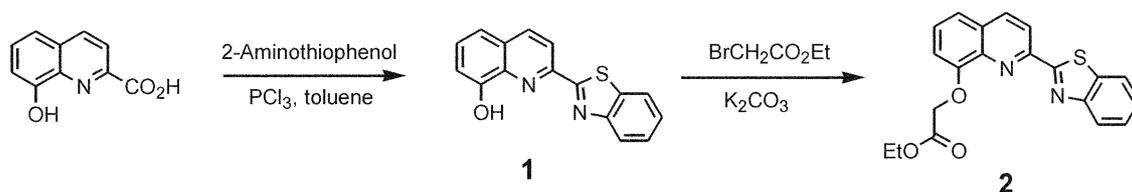
Introduction

In recent decades considerable efforts have been devoted to develop molecular sensing or recognizing systems for the chemically and biologically important metal ions and organic molecules.¹ Among many targeted systems, the detection of heavy metal ions is particular interesting due to their environmental and biological toxicities.²⁻⁴ Although many types of Hg²⁺ ion sensing ionophores have been introduced to detect mercuric ions in chemical and biological systems, there still needs more sensors for the analysis of this ion in varying types of samples in terms of the sample matrix and concentration ranges. Especially, the development of Hg²⁺-selective fluorescent chemosensors has been attracted increasing attentions because of the inherent advantage of high sensitivity and selectivity as well as providing real-time chemical analysis.⁵⁻⁷ 8-Hydroxyquinoline (8-HQ) moiety has received continuous attention as a platform for the construction of a number of selective and efficient ionophores.⁸ The most interesting feature of 8-HQ is its very low quantum yield in aqueous or organic solutions but the fluorescence enhancement occurred from cation binding and many metal chelates of 8-HQ exhibit intense fluorescences.^{9,10} Although the selectivity of 8-HQ and its simple derivative is rather poor, it can be improved by appropriate substitution on the phenolic oxygen atom or aromatic rings.¹¹ In this paper, we report the synthesis of

new 8-hydroxyquinoline derivatives having appended benzothiazole function and additional binding site of ester group on phenolic moiety and their ionophoric properties toward transition metal ions. The ester derivative **2** exhibited a pronounced Hg²⁺-selective ON-OFF type fluoroionophoric properties in aqueous dioxane solution.

Results and Discussion

The targeted compounds were designed by the modification of well-known 8-HQ moiety. In the first step, benzothiazole moiety was introduced at 2-position of quinoline to improve the fluorescence properties of 8-HQ backbone as well as to give an additional binding site of thiazole functional group for the complexation of specific metal ions. Secondly, modification of hydroxyl unit was also carried out in an attempt to improve the binding affinity for the target metal ions as well as to provide the possibility of the introduction of the present chelating subunit into other supramolecular systems. The syntheses of 8-HQ derivatives **1** and **2** are shown in Scheme 1. 8-Hydroxyquinoline-2-benzothiazole **1** was prepared by the condensation of 8-hydroxyquinoline-2-carboxylic acid with 2-aminothiophenol in the presence of phosphorus trichloride in toluene¹² (75% yield). The reaction of **1** with ethyl bromoacetate (K₂CO₃ in CH₃CN) gave compound **2** (72% yield).¹³ The structures of the prepared compounds were characterized by ¹H NMR,



Scheme 1

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^{13}C NMR, and HRMS.

The benzothiazole derivative **1** is weakly fluorescent in common organic solvents such as THF, dioxane, and CH_3CN . Generally, neutral 8-hydroxyquinoline has been known to be nonfluorescent in protic solvents due to the efficient radiationless relaxation to the ground state by intra- and intermolecular excited-state proton transfer.¹⁴ In dioxane- H_2O (9 : 1, v/v), **1** showed a weak blue fluorescence around 470 nm. The fluorescence of **1** was quenched upon the addition of metal ions by exhibiting responses in decreasing order of $\text{Hg}^{2+} > \text{Cu}^{2+} \approx \text{Pb}^{2+} \approx \text{Ni}^{2+} > \text{Zn}^{2+} \approx \text{Cd}^{2+} \approx \text{Co}^{2+} \gg$ alkaline earth metal ions. Unfortunately, the relatively weak fluorescence of **1** in the present case is further decreased by the treatment with metal ions, which is not desirable for the sensitive signaling purpose in the analysis of metal ions. The UV-Vis absorption spectra of **1** were also affected by the complexation with metal ions. Upon the addition of Hg^{2+} ions, the absorption band at 300 nm was shifted to 360 nm, while with other responding metal ions such as Cu^{2+} , Pb^{2+} , and Ni^{2+} ions, the absorption band at 300 nm was shifted to 330 nm. The colors of the solution of **1** in the presence of metal ions were changed from colorless to faint yellow for **1**- Hg^{2+} , to pink for **1**- Cu^{2+} , **1**- Cd^{2+} , **1**- Ni^{2+} , and **1**- Pb^{2+} complexes. However, the selective discrimination of **1** between Hg^{2+} , Cd^{2+} , Cu^{2+} , Ni^{2+} , and Pb^{2+} ions was not satisfactory for the application of 8-HQ derivative as ion-selective chemosensors.

As has been already mentioned, we have tried to modify the structure and ionophoric properties of **1** by the introduction of ester function onto phenolic hydroxyl group by alkylation, which could act as additional binding site for the targeted metal ions as well as a handle for the introduction of the present chelating unit to other chemical and biological systems.¹⁵ As expected, the fluorescence of quinoline moiety was enhanced by the alkylation of phenolic group and the ethyl ester derivative **2** showed intense blue fluorescence in common organic solvents in comparison with the observation that the ionophore **1** exhibited relatively weak fluorescence to investigate its binding ability towards metal ions.

Along with the improved fluorescence emission intensity, ethyl ester derivative **2** showed more selective ionophoric properties than **1** toward Hg^{2+} ions over other transition metal ions. In particular, in dioxane- H_2O (9 : 1, v/v) solution, the free ionophore **2** (3.0×10^{-5} M) showed an intense blue fluorescence around 455 nm ($\lambda_{\text{ex}} = 350$ nm). Upon interaction with metal ions of Mg^{2+} , Ca^{2+} , Ba^{2+} , Co^{2+} , Zn^{2+} , Cd^{2+} , and Pb^{2+} ions (in perchlorate), the emissions of **2** centered at 460 nm remained nearly unchanged (Figure 1). However, Hg^{2+} ions acted as the most effective quencher and the quenching efficiency was found to be larger than 98% with 100 equiv of added metal ions. Among other surveyed metal ions, Cu^{2+} ions also showed slight quenching effect of 14% in the presence of 100 equiv of metal ions. The selectivity was found to be decreased in the sequence of $\text{Hg}^{2+} \gg \text{Cu}^{2+} > \text{Cd}^{2+} > \text{Co}^{2+} \approx \text{Ni}^{2+} \approx \text{Pb}^{2+} \approx \text{Zn}^{2+}$.

Figure 2 illustrates the changes of fluorescence spectra of

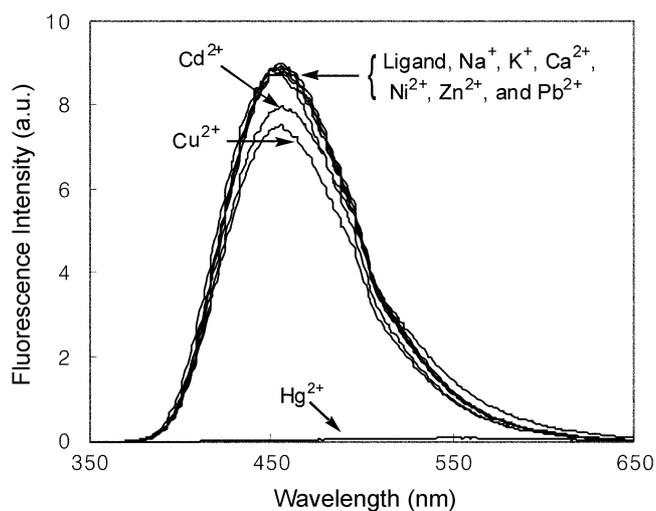


Figure 1. Fluorescence spectra of free **2** ($\lambda_{\text{ex}} = 350$ nm) and **2** in the presence of 100 equiv of metal perchlorates in dioxane- H_2O (9 : 1, v/v). $[\mathbf{2}] = 3.0 \times 10^{-5}$ M.

2 upon the addition of increasing amount of Hg^{2+} ions. The Job's plot for the complexation behavior revealed that the ester **2** formed complexes with Hg^{2+} ions in 1 : 1 (ligand **2** : Hg^{2+} ion) stoichiometry. The association constants (K_{assoc}) determined by the nonlinear curve fitting¹⁶ of the titration data were found to be $2.0 \times 10^4 \text{ M}^{-1}$ and $2.4 \times 10^2 \text{ M}^{-1}$ for Hg^{2+} and the most interfering metal ions of Cu^{2+} ions, respectively. The detection limit¹⁷ of **2** for the analysis of Hg^{2+} ions was also estimated to be 1.5×10^{-4} M from the titration data. Based on the observed Hg^{2+} ion selectivity of **2**, the competitive experiments have been carried out by the gradual addition of Hg^{2+} ions into the ionophore solution in the presence of 100 equiv of background metal ions of Mg^{2+} , Ca^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , and Pb^{2+} in their perchlorate salts. The ionophore **2** showed a clear Hg^{2+} dependent quenching behavior, although somewhat residual quenching of **2** due to the presence of a large amount of background metal ions was observed. The Hg^{2+} -sensitive fluorescence quenching behavior suggests that the compound **2** can be used as a selective probe for the analysis of Hg^{2+}

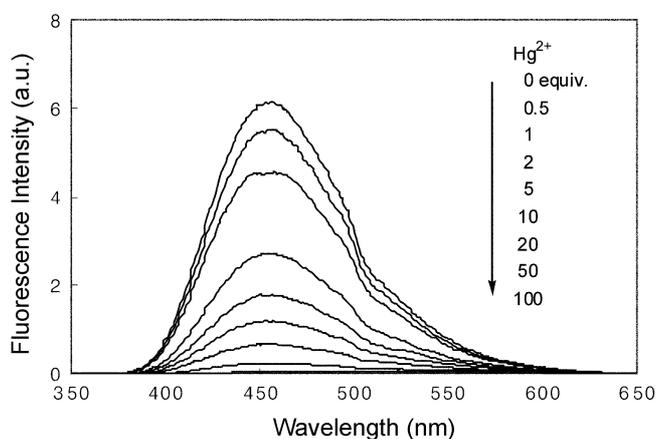


Figure 2. Fluorescence spectra of **2** in dioxane- H_2O (9 : 1, v/v) upon the addition of Hg^{2+} ions ($\lambda_{\text{ex}} = 350$ nm). $[\mathbf{2}] = 3.0 \times 10^{-5}$ M.

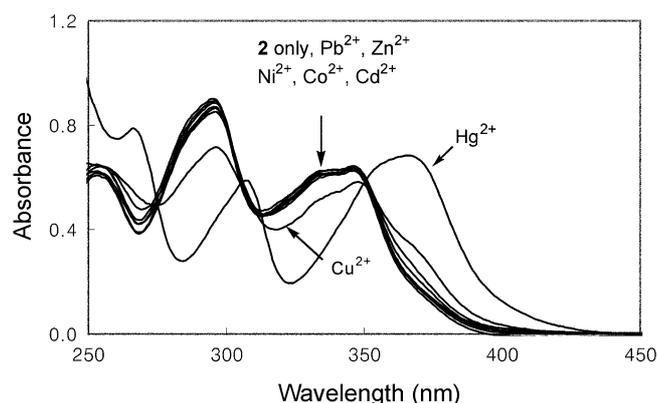


Figure 3. UV-Vis absorption spectra of free **2** and **2** in the presence of 100 equiv of metal perchlorates in dioxane-H₂O (9 : 1, v/v). [**2**] = 3.0×10^{-5} M.

ions in the presence of other common interfering metal ions. The selective complexation of **2** with Hg²⁺ ions was further evidenced by the FAB-mass measurements. A prominent peak at $m/z = 655.05$ corresponding to the complex of [2+Hg+ClO₄]⁺ was obtained under competitive condition with a mixture of Hg(ClO₄)₂ and other metal perchlorates (Cd²⁺, Co²⁺, Cu²⁺, Pb²⁺, and Zn²⁺) in *m*-nitrobenzyl alcohol (*m*-NBA).

Along with Hg²⁺-selective fluorogenic properties, the ionophore **2** also showed a selective chromogenic behavior towards Hg²⁺ ions. As shown in Figure 3, the UV-Vis absorption spectra of **2** showed Hg²⁺-selective spectral changes: the addition of Hg²⁺ ions resulted in significant bathochromic shift of absorption band of **2** from around 350 nm to 370 nm while those of other metal ions remained nearly unchanged except for a minor change for Cu²⁺ ions.

In summary, we have synthesized two 8-hydroxyquinoline derivatives having appended benzothiazole function and examined their ionophoric properties towards representative transition and heavy metal ions. The ester functionalized ionophore **2** exhibited a selective and sensitive fluorescence quenching behavior towards Hg²⁺ ions even in the presence of common interfering metal ions, which could be utilized as Hg²⁺-selective sensors in aqueous environment. The Hg²⁺-selective ON-OFF type fluorescence behavior could be utilized as a useful component for the construction of functional molecular switching systems.

Experimental Section

General. All manipulations were carried out under an inert atmosphere. All solvents were purchased from Aldrich Chemical Co. as 'anhydrous' or 'spectroscopic grade'. 8-Hydroxyquinoline-2-carboxylic acid and 2-aminothiophenol were purchased from Aldrich Chemical Co. ¹H and ¹³C NMR spectra were measured on a Varian Gemini-2000 spectrometer. HRMS and FAB mass spectra (in *m*-NBA matrix) were obtained with a Micromass Autospec Mass Spectrometer. UV spectra were measured using a JASCO V-550 spectrophotometer. Fluorescence spectra were obtained

using an Aminco-Bowman Series 2 Spectrophotometer.

Preparation of 8-Hydroxyquinoline Benzothiazole 1. 2-Aminothiophenol (138 mg, 1.1 mmol) and 8-hydroxyquinoline-2-carboxylic acid (190 mg, 1 mmol) were dissolved in dry toluene. The solution was warmed to 40 °C, and equimolar amount of phosphorus trichloride (0.1 mL, 1.1 mmol) was added dropwise to the reaction mixture. The mixture was heated 100 °C for 4 h and then cooled to room temperature. The reaction mixture was extracted with 20% sodium carbonate solution and washed with distilled water, and then evaporated to produce solid residue. The crude product was crystallized in dichloromethane/hexane to give 8-hydroxyquinoline-2-benzothiazole **1** in 75% yield. mp 189-191 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.51 (d, *J* = 8.7 Hz, 1H), 8.32 (d, *J* = 8.7 Hz, 1H), 8.16 (d, *J* = 8.1 Hz, 1H), 8.05 (s, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.54-7.24 (m, 4H), 7.24 (d, *J* = 7.5 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 152.5, 137.5, 129.5, 129.3, 126.7, 126.3, 124.1, 119.3, 118.3, 111.2; HRMS (EI); *m/z* calcd for C₁₆H₁₀N₂OS 278.0511 Found 278.04783.

Preparation of Ester Derivative of 8-Hydroxyquinoline Benzothiazole 2. To the mixture of benzothiazole **1** (140 mg, 0.5 mmol) and K₂CO₃ (138 mg, 1 mmol) in CH₃CN was added ethyl bromoacetate (120 mg, 0.7 mmol) and the reaction mixture was heated under reflux for 48 h. After which the mixture was evaporated, dissolved in dichloromethane, and washed with water. The organic layer was evaporated under reduced pressure and the residue was purified by recrystallization from CH₂Cl₂-MeOH to yield ester derivative **2** (130 mg). Yield: 72%; ¹H NMR (300 MHz, CDCl₃) δ 8.51 (d, *J* = 8.7 Hz, 1H), 8.30 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.55-7.16 (m, 5H), 5.10 (s, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.3, 169.3, 154.7, 154.1, 150.5, 140.5, 137.4, 136.8, 130.6, 127.9, 126.5, 126.1, 124.0, 122.3, 121.7, 119.0, 113.6, 67.8, 61.5, 14.3; HRMS (EI); *m/z* calcd for C₂₀H₁₆N₂O₃S 364.0882 Found 364.0888.

Fluorescence Titration Experiments. All the solvents used were spectroscopic grade. Incremental amounts of metal perchlorate solutions (2.0×10^{-2} M in H₂O) were added to the ionophore solution (2.0×10^{-4} M in dioxane) by micropipette. After this, calculated amounts of solvents were added to make the required concentrations of the ionophore and metal ions, as well as the solvent compositions.

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